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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| (21) International Application Number: PCT/US97/20804  |  |           | <p>Francisco, CA 94122 (US). LATIMER, Lee, H. [US/US]; 56 Sheridan Road, Oakland, CA 94618 (US). MABRY, Thomas, E. [US/US]; 8104 Hi-Vu Drive, Indianapolis, IN 46227 (US). NISSEN, Jeffrey, S. [US/US]; 4348 Oil Creek Drive, Indianapolis, IN 46268 (US). PORTER, Warren, J. [US/US]; 8037 Lieber Road, Indianapolis, IN 46260 (US). REEL, Jon, K. [US/US]; 14701 Alsong Court, Carmel, IN 46032 (US). THORSETT, Eugene, D. [US/US]; 571 Buena Vista Street, Moss Beach, CA 94038 (US). TUNG, Jay, S. [US/US]; 2224 Semeria Avenue, Belmont, CA 94002 (US). WU, Jing [CN/US]; Apartment 502, 10 De Sabla Road, San Mateo, CA 94402 (US). EID, Clark, Norman [US/US]; 53 Dundee Drive, Cheshire, CT 06410 (US). SCOTT, William, Leonard [US/US]; 144 Buckingham Drive, Indianapolis, IN 46208 (US).</p> <p>(74) Agents: SWISS, Gerald, F. et al.; Burns, Doane, Swecker &amp; Mathis, L.L.P., P.O. Box 1404, Alexandria, VA 22313-1404 (US).</p> <p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b><br/>Without international search report and to be republished upon receipt of that report.</p> |
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| (54) Title: METHODS AND COMPOUNDS FOR INHIBITING $\beta$ -AMYLOID PEPTIDE RELEASE AND/OR ITS SYNTHESIS   |  |           |   |
| (57) Abstract  |  |           |   |
| <p>Disclosed are compounds which inhibit <math>\beta</math>-amyloid peptide release and/or its synthesis, and, accordingly, have utility in treating Alzheimer's disease. Also disclosed pharmaceutical compositions comprising a compound which inhibits <math>\beta</math>-amyloid peptide release and/or its synthesis as well as methods for treating Alzheimer's disease both prophylactically and therapeutically with such pharmaceutical compositions.</p>                 |  |           |   |

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## METHODS AND COMPOUNDS FOR INHIBITING $\beta$ -AMYLOID PEPTIDE RELEASE AND/OR ITS SYNTHESIS

### CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of the following U.S. Provisional Applications:

1. U.S. Provisional Application No. 60/\_\_\_\_,\_\_\_\_, which was converted  
5 pursuant to 37 C.F.R. §1.53(b)(2)(ii) from U.S. Patent Application No. 08/755,442,  
filed November 22, 1996;
2. U.S. Provisional Application No. 60/\_\_\_\_,\_\_\_\_, which was converted  
pursuant to 37 C.F.R. §1.53(b)(2)(ii) from U.S. Patent Application No. 08/808,528,  
filed February 28, 1997;
- 10 3. U.S. Provisional Application No. 60/\_\_\_\_,\_\_\_\_, which was converted  
pursuant to 37 C.F.R. §1.53(b)(2)(ii) from U.S. Patent Application No. 08/807,528,  
filed February 28, 1997; and
4. U.S. Provisional Application No. 60/\_\_\_\_,\_\_\_\_, which was converted  
pursuant to 37 C.F.R. §1.53(b)(2)(ii) from U.S. Patent Application No. 08/807,427,  
15 filed February 28, 1997.

Each of these applications are incorporated herein by reference in their entirety.

### BACKGROUND OF THE INVENTION

#### 20 Field of the Invention

This invention relates to methods which inhibit cellular  $\beta$ -amyloid peptide release and/or its synthesis, and, accordingly, have utility in treating Alzheimer's disease. This invention also relates to pharmaceutical compositions comprising such compounds as well as methods for inhibiting release of  
25  $\beta$ -amyloid peptide.

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## BACKGROUND OF THE INVENTION

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This invention relates to methods which inhibit cellular  $\beta$ -amyloid peptide release and/or its synthesis, and, accordingly, have utility in treating Alzheimer's disease. This invention also relates to pharmaceutical compositions comprising such compounds as well as methods for inhibiting release of  $\beta$ -amyloid peptide.

### References

The following publications, patents and patent applications are cited in this application as superscript numbers:

- <sup>1</sup> Glenner, et al., "Alzheimer's Disease: Initial Report of the Purification and Characterization of a Novel Cerebrovascular Amyloid Protein", *Biochem. Biophys. Res. Commun.*, 120:885-890 (1984).
- <sup>2</sup> Glenner, et al., "Polypeptide Marker for Alzheimer's Disease and its Use for Diagnosis", *U.S. Patent No. 4,666,829* issued May 19, 1987.
- <sup>3</sup> Selkoe, "The Molecular Pathology of Alzheimer's Disease", *Neuron*, 6:487-498 (1991).
- <sup>4</sup> Goate, et al., "Segregation of a Missense Mutation in the Amyloid Precursor Protein Gene with Familial Alzheimer's Disease", *Nature*, 349:704-706 (1990).
- <sup>5</sup> Chartier-Harlin, et al., "Early-Onset Alzheimer's Disease Caused by Mutations at Codon 717 of the  $\beta$ -Amyloid Precursor Protein Gene", *Nature*, 353:844-846 (1989).
- <sup>6</sup> Murrell, et al., "A Mutation in the Amyloid Precursor Protein Associated with Hereditary Alzheimer's Disease", *Science*, 254:97-99 (1991).
- <sup>7</sup> Mullan, et al., "A Pathogenic Mutation for Probable Alzheimer's Disease in the APP Gene at the N-Terminus of  $\beta$ -Amyloid", *Nature Genet.*, 1:345-347 (1992).

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- 8        Schenk, et al., "Methods and Compositions for the Detection of Soluble  $\beta$ -Amyloid Peptide", *International Patent Application Publication No. WO 94/10569*, published 11 May 1994.
- 5        9        Selkoe, "Amyloid Protein and Alzheimer's Disease", *Scientific American*, pp. 2-8, November, 1991.
- 10       10       Losse, et al., *Tetrahedron*, 27:1423-1434 (1971).
- 10       11       Citron, et al., "Mutation of the  $\beta$ -Amyloid Precursor Protein in Familial Alzheimer's Disease Increases  $\beta$ -Protein Production, *Nature*, 360:672-674 (1992).
- 15       12       Hansen, et al., "Reexamination and Further Development of a Precise and Rapid Dye Method for Measuring Cell Growth/Cell Kill", *J. Immun. Meth.*, 119:203-210 (1989).
- 13       13       P. Seubert, *Nature* (1992) 359:325-327
- 20       14       Johnson-Wood et al., *PNAS USA* (1997) 94:1550-1555
- 15       15       *Tetrahedron Letters*, 34(48), 7685 (1993))

25       All of the above publications, patents and patent applications are herein incorporated by reference in their entirety to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference in its entirety.

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#### State of the Art

Alzheimer's Disease (AD) is a degenerative brain disorder characterized clinically by progressive loss of memory, cognition, reasoning, judgment and emotional stability that gradually leads to profound mental deterioration and ultimately death. AD is a very common cause of progressive mental failure (dementia) in aged humans and is believed to represent the fourth most common medical cause of death in the United States. AD has been observed in races and ethnic groups worldwide and presents a major present and future public health problem. The disease is currently estimated to affect about two to three

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million individuals in the United States alone. AD is at present incurable. No treatment that effectively prevents AD or reverses its symptoms and course is currently known.

5           The brains of individuals with AD exhibit characteristic lesions termed senile (or amyloid) plaques, amyloid angiopathy (amyloid deposits in blood vessels) and neurofibrillary tangles. Large numbers of these lesions, particularly amyloid plaques and neurofibrillary tangles, are generally found in several areas of the human brain important for memory and cognitive function  
10 in patients with AD. Smaller numbers of these lesions in a more restrictive anatomical distribution are also found in the brains of most aged humans who do not have clinical AD. Amyloid plaques and amyloid angiopathy also characterize the brains of individuals with Trisomy 21 (Down's Syndrome) and Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch Type  
15 (HCHWA-D). At present, a definitive diagnosis of AD usually requires observing the aforementioned lesions in the brain tissue of patients who have died with the disease or, rarely, in small biopsied samples of brain tissue taken during an invasive neurosurgical procedure.

20           The principal chemical constituent of the amyloid plaques and vascular amyloid deposits (amyloid angiopathy) characteristic of AD and the other disorders mentioned above is an approximately 4.2 kilodalton (kD) protein of about 39-43 amino acids designated the  $\beta$ -amyloid peptide ( $\beta$ AP) or sometimes  $A\beta$ ,  $A\beta P$  or  $\beta/A4$ .  $\beta$ -Amyloid peptide was first purified and a partial amino  
25 acid sequence was provided by Glenner, et al.<sup>1</sup> The isolation procedure and the sequence data for the first 28 amino acids are described in U.S. Patent No. 4,666,829<sup>2</sup>.

30           Molecular biological and protein chemical analyses have shown that the  $\beta$ -amyloid peptide is a small fragment of a much larger precursor protein (APP), that is normally produced by cells in many tissues of various animals,

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including humans. Knowledge of the structure of the gene encoding the APP has demonstrated that  $\beta$ -amyloid peptide arises as a peptide fragment that is cleaved from APP by protease enzyme(s). The precise biochemical mechanism by which the  $\beta$ -amyloid peptide fragment is cleaved from APP and subsequently deposited as amyloid plaques in the cerebral tissue and in the walls of the cerebral and meningeal blood vessels is currently unknown.

Several lines of evidence indicate that progressive cerebral deposition of  $\beta$ -amyloid peptide plays a seminal role in the pathogenesis of AD and can precede cognitive symptoms by years or decades. See, for example, Selkoe<sup>3</sup>. The most important line of evidence is the discovery that missense DNA mutations at amino acid 717 of the 770-amino acid isoform of APP can be found in affected members but not unaffected members of several families with a genetically determined (familial) form of AD (Goate, et al.<sup>4</sup>; Chartier-Harlan, et al.<sup>5</sup>; and Murrell, et al.<sup>6</sup>) and is referred to as the Swedish variant. A double mutation changing lysine<sup>595</sup>-methionine<sup>596</sup> to asparagine<sup>595</sup>-leucine<sup>596</sup> (with reference to the 695 isoform) found in a Swedish family was reported in 1992 (Mullan, et al.<sup>7</sup>). Genetic linkage analyses have demonstrated that these mutations, as well as certain other mutations in the APP gene, are the specific molecular cause of AD in the affected members of such families. In addition, a mutation at amino acid 693 of the 770-amino acid isoform of APP has been identified as the cause of the  $\beta$ -amyloid peptide deposition disease, HCHWA-D, and a change from alanine to glycine at amino acid 692 appears to cause a phenotype that resembles AD in some patients but HCHWA-D in others. The discovery of these and other mutations in APP in genetically based cases of AD prove that alteration of APP and subsequent deposition of its  $\beta$ -amyloid peptide fragment can cause AD.

Despite the progress which has been made in understanding the underlying mechanisms of AD and other  $\beta$ -amyloid peptide related diseases, there remains a need to develop methods and compositions for treatment of the



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disease(s). Ideally, the treatment methods would advantageously be based on drugs which are capable of inhibiting  $\beta$ -amyloid peptide release and/or its synthesis *in vivo*.

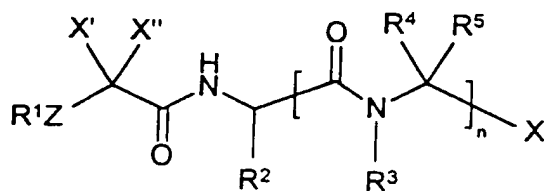
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### SUMMARY OF THE INVENTION

This invention is directed to the discovery of a class of compounds which inhibit  $\beta$ -amyloid peptide release and/or its synthesis and, therefore, are useful in the prevention of AD in patients susceptible to AD and/or in the treatment of patients with AD in order to inhibit further deterioration in their condition. The class of compounds having the described properties are defined by formula I below:

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I

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wherein  $\text{R}^1$  is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic;

$\text{R}^2$  is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, aryl, heteroaryl and heterocyclic;

each  $\text{R}^3$  is independently selected from the group consisting of hydrogen and methyl and  $\text{R}^3$  together with  $\text{R}^4$  can be fused to form a cyclic structure of from 3 to 8 atoms which is optionally fused with an aryl or heteroaryl group;

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each  $R^4$  is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, heteroaryl, heterocyclic, substituted alkyl, substituted alkenyl and substituted alkynyl;

5 each  $R^5$  is selected from hydrogen and methyl or together with  $R^4$  forms a cycloalkyl group of from 3 to 6 carbon atoms;

X is selected from the group consisting of  $-C(O)Y$  and  $-C(S)Y$  where Y is selected from the group consisting of

(a) alkyl or cycloalkyl,

10 (b) substituted alkyl with the proviso that the substitution on said substituted alkyl do not include  $\alpha$ -haloalkyl,  $\alpha$ -diazoalkyl,  $\alpha$ -OC(O)alkyl, or  $\alpha$ -OC(O)aryl groups,

(c) alkoxy or thioalkoxy,

(d) substituted alkoxy or substituted thioalkoxy,

(e) hydroxy,

15 (f) aryl,

(g) heteroaryl,

(h) heterocyclic,

20 (i)  $-NR'R''$  where  $R'$  and  $R''$  are independently selected from hydrogen, alkyl, alkenyl, alkynyl, substituted alkyl, substituted alkenyl, substituted alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclic, where one of  $R'$  or  $R''$  is hydroxy or alkoxy, and where  $R'$  and  $R''$  are joined to form a cyclic group having from 2 to 8 carbon atoms optionally containing 1 to 2 additional heteroatoms selected from oxygen, sulfur and nitrogen and optionally substituted with one or more alkyl, alkoxy or carboxylalkyl groups,

25 (j)  $-NHSO_2-R^8$  where  $R^8$  is selected from alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, aryl, heteroaryl and heterocyclic,

(k)  $-NR^9NR^{10}R^{10}$  where  $R^9$  is hydrogen or alkyl, and each  $R^{10}$  is independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclic, and

30 (l)  $-ONR^9[C(O)O]_zR^{10}$  where  $z$  is zero or one,  $R^9$  and  $R^{10}$  are as defined above;

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X can also be  $-CR^6R^6Y'$  where each  $R^6$  is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl and heterocyclic and  $Y'$  is selected from the group consisting of hydroxyl, amino, thiol, alkoxy, substituted alkoxy, thioalkoxy, substituted thioalkoxy,  $-OC(O)R^7$ ,  $-SSR^7$ ,  $-SSC(O)R^7$  where  $R^7$  is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl and heterocyclic,

$X'$  is hydrogen, hydroxy, or fluoro;

$X''$  is hydrogen, hydroxy or fluoro, or  $X'$  and  $X''$  together form an oxo group,

$Z$  is selected from the group consisting of a bond covalently linking  $R^1$  to  $-CX'X''-$ , oxygen and sulfur;

$n$  is an integer equal to 1 or 2; and

pharmaceutically acceptable salts thereof

with the provisos that:

A. when  $R^1$  is phenyl or 3-nitrophenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^4$  is  $-\text{CH}(\text{OH})\text{CH}_3$ ,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen,  $Z$  is a bond, and  $n$  is 1, then  $X$  is not  $-\text{C}(\text{O})\text{OH}$ ;

B. when  $R^1$  is phenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^4$  is  $-\text{CH}(\text{OH})\text{CH}_3$  derived from D-threonine,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen,  $Z$  is a bond, and  $n$  is 1, then  $X$  is not  $-\text{C}(\text{O})\text{OH}$  or  $-\text{C}(\text{O})\text{OCH}_3$ ;

C. when  $R^1$  is phenyl,  $R^2$  is methyl,  $R^4$  is benzyl,  $R^5$  is hydrogen,  $X$  is methoxycarbonyl,  $X'$  and  $X''$  are hydrogen,  $Z$  is a bond, and  $n$  is 1, then  $R^3$  is not methyl;

D. when  $R^1$  is *iso*-propyl,  $R^2$  is  $-\text{CH}_2\text{C}(\text{O})\text{NH}_2$ ,  $R^3$  is hydrogen,  $R^4$  is *iso*-butyl,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen,  $Z$  is a bond, and  $n$  is 1, then  $X$  is not  $-\text{C}(\text{O})\text{OCH}_3$ ;

E. when  $R^1$  is phenyl,  $R^2$  is methyl,  $R^5$  is hydrogen,  $X$  is  $-\text{C}(\text{O})\text{OCH}_3$ ,  $X'$  and  $X''$  are hydrogen,  $Z$  is a bond, and  $n$  is 1, then  $R^3$ , the nitrogen atom attached to  $R^3$ , and  $R^4$  do not form 1,2,3,4-tetrahydro*iso*-quinolin-2-yl or pyrrolidin-2-yl;

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F. when  $R^1$  is phenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^5$  is hydrogen, X is  $-C(O)OCH_3$ ,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then  $R^4$  is not 4-amino-*n*-butyl;

5 G. when  $R^1$  is 3-nitrophenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^4$  is  $-CH(OH)CH_3$ ,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then X is not  $-C(O)NH_2$  or  $-CH_2OH$ ;

H. when  $R^1$  is phenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^5$  is hydrogen, X is  $-CH_2OCH_3$ ,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then  $R^4$  is not benzyl or ethyl;

10 I. when  $R^1$  is 3,5-difluorophenyl,  $R^2$  is methyl,  $R^3$  is methyl,  $R^4$  is methyl,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then X is not  $-CHOH\phi$ ;

J. when  $R^1$  is 3,5-difluorophenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^4$  is phenyl derived from D-phenylglycine,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then X is not  $-CHOH\phi$  or  $-CH_2OH$ ;

15 K. when  $R_1$  is *N*-(2-pyrrolidinonyl),  $R_2$  is methyl,  $R_3$  is hydrogen,  $R_4$  is benzyl,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then X is not  $-C(O)OCH_3$ ;

L. when  $R^1$  is 3,5-difluorophenyl,  $R^2$  is methyl derived from D-alanine,  $R^3$  is hydrogen,  $R^4$  is phenyl derived from D-phenylglycine,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then X is not  $-C(O)NH$ -benzyl;

M. when  $R^1$  is 3,5-difluorophenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^4$  is hydrogen,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then X is not  $-CH_2OH$ ;

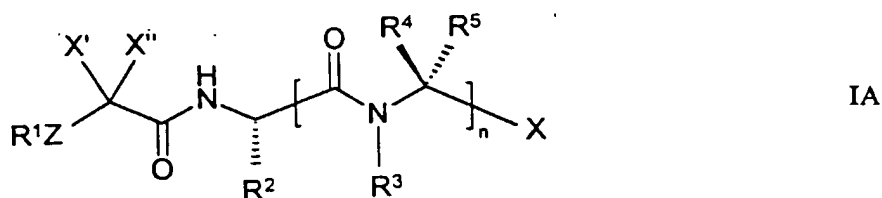
25 N. when  $R^1$  is 3,5-difluorophenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^4$  is 4-phenylphenyl,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then X is not  $-C(O)NHC(CH_3)_3$ ; and

O. when  $R^1$  is 3,5-difluorophenyl,  $R^2$  is methyl,  $R^3$  is hydrogen,  $R^4$  is phenyl derived from D-phenylglycine,  $R^5$  is hydrogen,  $X'$  and  $X''$  are hydrogen, Z is a bond, and  $n$  is 1, then X is not  $-C(O)NHCH(CH_3)\phi$ .

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Preferably, the compounds of this invention are derived from L-amino acids and, accordingly, are represented by formula IA:



Accordingly, in one of its method aspects, this invention is directed to a method for inhibiting  $\beta$ -amyloid peptide release and/or its synthesis in a cell which method comprises administering to such a cell an amount of a compound or a mixture of compounds of formula I above effective in inhibiting the cellular release and/or synthesis of  $\beta$ -amyloid peptide.

Because the *in vivo* generation of  $\beta$ -amyloid peptide is associated with the pathogenesis of AD<sup>8,9</sup>, the compounds of formula I can also be employed in conjunction with a pharmaceutical composition to prophylactically and/or therapeutically prevent and/or treat AD. Accordingly, in another of its method aspects, this invention is directed to a prophylactic method for preventing the onset of AD in a patient at risk for developing AD which method comprises administering to said patient a pharmaceutical composition comprising a pharmaceutically inert carrier and an effective amount of a compound or a mixture of compounds of formula I above.

In yet another of its method aspects, this invention is directed to a therapeutic method for treating a patient with AD in order to inhibit further deterioration in the condition of that patient which method comprises

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administering to said patient a pharmaceutical composition comprising a pharmaceutically inert carrier and an effective amount of a compound or a mixture of compounds of formula I above.

5           Compounds suitable for use in the claimed methods include, by way of example only, the following:

- 10           *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-aminohexanoate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-histidine methyl ester
- N*-benzyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-aminohexanamide
- 15           *N*-2-(*N,N*-dimethylamino)ethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-aminohexanamide
- N*-(2-methoxyethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-aminohexanamide
- 20           *N*-2-(*N,N*-dimethylamino)ethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalaninamide
- N*-(4-pyridyl)methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalaninamide
- 25           *N*-(3-pyridyl)methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalaninamide
- N*-(4-pyridyl)methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-aminohexanamide
- 30           *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-aminohexanoate *tert*-butyl ester
- N*-[*N*-(pent-4-enoyl)-*L*-alaninyl]-*L*-phenylalanine methyl ester
- N*-[*N*-(dec-4-enoyl)-*L*-alaninyl]-*L*-phenylalanine methyl ester
- 40           *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-4-[3-(*N,N*-dimethylamino)propoxy]phenylalanine methyl ester

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- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-[(*tert*-butyloxycarbonyl)methoxy]phenylalanine methyl ester
- 5 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-tyrosine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-(carboxymethoxy)phenylalanine methyl ester
- 10 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-(2-morpholinoethoxy)phenylalanine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-6-(*N,N*-dimethylamino)hexanoate methyl ester
- 15 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-3-(2-pyridyl)propionate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-3-(3-pyridyl)propionate methyl ester
- 20 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-proline methyl ester
- 1-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]piperidine-2-carboxylate methyl ester
- 25 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-3-(4-pyridyl)propionate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-3-methoxypropionate methyl ester
- 30 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-3-morpholinopropionate methyl ester
- N*-(2-methoxyethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-(2-morpholinoethoxy)phenylalaninamide
- 35 *N*-(2-methoxyethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-3-methoxypropionamide
- 40 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]glycine methyl ester
- N*-(2-methoxyethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-3-(4-pyridyl)propionamide
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- N*-(2-methoxyethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-2-amino-3-(2-pyridyl)propionamide
- 5      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-amino-3-(thiazol-4-yl)propionate methyl ester
- 2-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylate methyl ester
- 10      *N*-(3-methoxybenzyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalaninamide
- 15      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-amino-3-(1-naphthyl)propionate methyl ester
- 20      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-amino-3-(2-naphthyl)propionate methyl ester
- 25      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-amino-3-(2-thienyl)propionate methyl ester
- 30      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalanine benzyl ester
- 35      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalanine 3-bromopropyl ester
- 40      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalanine 3-iodopropyl ester
- 45      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-leucine *tert*-butyl ester
- 50      *N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-2-amino-2-(2-pyridyl)acetamide
- 55      *N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-2-amino-2-(3-pyridyl)acetamide
- 60      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*N*<sub>i</sub>-(*tert*-butoxycarbonyl)-*L*-lysine methyl ester
- 65      methyl *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-amino-4-phenylbutanoate
- 70      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]glycine 2-phenylethyl ester
- 75      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]glycine 3-phenylpropyl ester



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- N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(4-pyridyl)acetamide
- 5 *N*-[*N*-(phenylacetyl)-L-alaninyl]-L-threonine methyl ester
- N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-leucinamide
- N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-alaninamide
- 10 *N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-phenylalaninamide
- N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-valinamide
- 15 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(3-pyridyl)acetate ethyl ester
- N*-methyl-*N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-leucinamide
- N,N*-dimethyl-*N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-phenylalaninamide
- 20 *N,N*-dimethyl-*N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-leucinamide
- N,N*-dimethyl-*N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-valinamide
- 25 *N*-methyl-*N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-phenylalaninamide
- N*-methyl-*N'*-[*N*-(phenylacetyl)-L-alaninyl]-L-valinamide
- 30 *N*-methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-aminohexanamide
- N,N*-dimethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-aminohexanamide
- 35 *N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-aminohexanamide
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(3-methoxyphenyl)acetate methyl ester
- 40 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(4-methoxyphenyl)acetate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(2-pyridyl)acetate ethyl ester
- 45

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- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(4-pyridyl)acetate ethyl ester
- 5 *N*-[*N*-(cyclohexylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- N*-[*N*-(cyclopentylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- N*-[*N*-(cyclohex-1-enylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- 10 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-1-aminocyclopropane-1-carboxylate methyl ester
- N*-2-(*N,N*-dimethylamino)ethyl-*N*-methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 15 *N*-[*N*-(cyclopropylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]glycine benzyl ester
- 20 *N*-[*N*-(isovaleryl)-L-phenylglyciny]l]-L-alanine ethyl ester
- N*-[*N*-(3-nitrophenylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- N*-[*N*-(3-nitrophenylacetyl)-L-alaninyl]-L-alanine ethyl ester
- 25 *N*-[*N*-(3-nitrophenylacetyl)-L-alaninyl]glycine ethyl ester
- N*-hydroxy-*N'*-[*N*-(3-nitrophenylacetyl)-L-alaninyl]-D,L-threoninamide
- 30 *N*-[*N*-(isovaleryl)-L-phenylglyciny]l]-L-alanine *iso*-butyl ester
- N*-[*N*-(3-nitrophenylacetyl)-L-alaninyl]-2-amino-3-(3-hydroxyphenyl)propionate methyl ester
- 35 *N*-[*N*-(3-nitrophenylacetyl)-L-alaninyl]-L-tyrosine ethyl ester
- N*-[*N*-(isovaleryl)-L-isoleuciny]l]-L-alanine *iso*-butyl ester
- N*-[*N*-[*N*-(isovaleryl)-L-valiny]l]-L-phenylglyciny]l]-L-alanine *iso*-butyl ester
- 40 ester
- N*-[*N*-(isovaleryl)-L-phenylalaniny]l]-L-alanine *iso*-butyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alanine ethyl ester
- 45

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- 1-[*N*-(3-nitrophenylacetyl)-L-alaninyl]-indoline-(S)-2-carboxylate ethyl ester
- 5 *N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- N*-methoxy-*N*-methyl-*N'*-[*N*-(isovaleryl)-L-phenylglycinyl]-L-alaninamide
- N*-iso-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 10 *N,N*-di-*n*-propyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-valinamide
- 15 *N*-(4-nitrophenyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- N'*-[*N*-(isovaleryl)-L-phenylglycinyl]-L-alaninyl]-L-phenylalaninamide
- 20 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylalaninamide
- N*-iso-butyl-*N'*-[*N*-(isovaleryl)-L-phenylglycinyl]-L-alaninamide
- 25 *N*-(2-methoxyethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylalaninamide
- N*-(4-nitrobenzyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 30 *N*-(4-nitrophenyl)-*N'*-[*N*-(isovaleryl)-L-phenylglycinyl]-L-alaninyl]-L-alaninamide
- 35 *N*-(4-nitrophenyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylalaninamide
- N*-benzyl-*N*-methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 40 *N*-(3,5-difluorobenzyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 45 *N*-(3-nitrobenzyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide

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- N*-benzyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-alaninamide
- N*-(4-nitrobenzyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalaninamide
- 5 *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-tryptophan methyl ester
- N*-(4-methoxybenzyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-alaninamide
- 10 *N*-[*N*-(phenylacetyl)-*L*-phenylglycinyl]-*L*-alanine ethyl ester
- N*-[*N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalaninyl]-*L*-phenylglycine methyl ester
- 15 *N*-[*N*-(cyclohexylacetyl)-*L*-phenylglycinyl]-*L*-alanine ethyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylglycine methyl ester
- 20 *N*-[*N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-alaninyl]-*L*-phenylglycine methyl ester
- N*-(2-phenylethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-alaninamide
- 25 *N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-tryptophanamide
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-amino-3-cyclohexylpropionate methyl ester
- 30 *N*-(2-methoxyethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-(*S*)-2-amino-3-(4-nitrophenyl)propionamide
- N*-[*N*-(3-nitrophenylacetyl)-*L*-alaninyl]-*L*-serine ethyl ester
- 35 *N*-[(*R*)- $\alpha$ -methylbenzyl]-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-alaninamide
- N*-[(*S*)- $\alpha$ -methylbenzyl]-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-alaninamide
- 40 *N*-(4-fluorobenzyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-alaninamide
- N*-(4-pyridylmethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-alaninamide
- 45

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- N*-(4-trifluoromethylbenzyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 5      *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-phenylpropionate ethyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylalanine *tert*-butyl ester
- 10     *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-methylpropionate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-cyclohexylacetate ethyl ester
- 15     *N*-(2-methoxyethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- N*-[*N*-(isovaleryl)-2-amino-2-cyclohexylacetyl]-L-alanine ethyl ester
- 20     *N*-2-(*N,N*-dimethylamino)ethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- N*-(2-pyridylmethyl)-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- 25     *N*-[*N*-(3-pyridylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- N*-[*N*-(2-pyridylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- 30     *N*-[*N*-(4-pyridylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(4-fluorophenyl)acetate ethyl ester
- 35     *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(2-fluorophenyl)acetate ethyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-phenylglycinyl]-L-alanine ethyl ester
- 40     *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-3-phthalimidopropionate ethyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycine neopentyl ester
- 45

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- N-tert-butyl-N'-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide*
- 5 *N-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycine tert-butyl ester*
- N'-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide*
- 10 *4-[N-[N-(3-nitrophenylacetyl)-L-alaninyl]-L-valinyl]morpholine*
- N-[N-(3-nitrophenylacetyl)-L-alaninyl]-L-valine ethyl ester*
- N-[N-(3-nitrophenylacetyl)-L-alaninyl]-L-threonine methyl ester*
- 15 *N-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-aminopentanoate methyl ester*
- 4-[N-[N-(3-nitrophenylacetyl)-L-alaninyl]-(S)-2-amino-3-tert-butoxybutyryl]morpholine*
- 20 *4-[N-[N-(3-nitrophenylacetyl)-L-alaninyl]-L-isoleucinyl]morpholine*
- N-[N-(3-nitrophenylacetyl)-L-alaninyl]-L-isoleucine methyl ester*
- 25 *N-[N-(3-nitrophenylacetyl)-L-alaninyl]-L-isoleucine*
- N-[N-[N-(3-nitrophenylacetyl)-L-alaninyl]-L-threoninyl]-L-valine ethyl ester*
- 30 *N-[N-(3-nitrophenylacetyl)-L-alaninyl]-(S)-2-aminopentanoate methyl ester*
- N-[N-(3-nitrophenylacetyl)-L-alaninyl]-L-leucine methyl ester*
- 35 *N-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-L-leucine methyl ester*
- N-2-methoxyethyl-N'-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide*
- 40 *N-2-(N,N-dimethylamino)ethyl-N'-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide*
- N-cyclohexyl-N'-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide*
- 45 *N-neopentyl-N'-[N-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide*

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- N*-tetrahydrofurfuryl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 5      *N*-2-pyridylmethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 3-[*N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninyl]thiazolidine
- 10      *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(*S*)-2-aminobutanoate methyl ester
- N*-[*N*-(3-nitrophenylacetyl)-L-alaninyl]-(*S*)-2-aminobutanoate methyl ester
- 15      *N*-(*R*)-*sec*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- 1-[*N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninyl]pyrrolidine
- 20      *N*-(*S*)-*sec*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-valine methyl ester
- 25      *N*-2-fluoroethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide
- N*-[(*S*)-6-methyl-3-oxohept-2-yl]-*N'*-(3,5-difluorophenylacetyl)-L-alaninamide
- 30      *N*-4-nitrobenzyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(*S*)-2-aminobutyramide
- N*-4-nitrobenzyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(*S*)-2-aminopentanamide
- 35      *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(3-fluorophenyl)acetate methyl ester
- N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(*S*)-2-amino-2-(2-thienyl)acetamide
- 40      *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(5-chlorobenzothiophen-2-yl)acetate methyl ester
- 45      *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(benzothiophen-2-yl)acetate ethyl ester

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- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(benzothiophen-3-yl)acetate methyl ester
- 5 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(2-thienyl)acetate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(benzothiophen-5-yl)acetate ethyl ester
- 10 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-2-(2-thienyl)acetate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-2-(2-thienyl)acetate *tert*-butyl ester
- 15 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-2-(2-thienyl)acetic acid
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(1*H*-tetrazol-5-yl)acetate methyl ester
- 20 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-2-(6-methoxy-2-naphthyl)acetate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(3-trifluoromethylphenyl)acetate methyl ester
- 25 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(4,5,6,7-tetrahydrobenzothiophen-2-yl)acetate methyl ester
- 30 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(thieno[2,3-*b*]thiophen-2-yl)acetate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-2-(2-methylthiazol-4-yl)acetate methyl ester
- 35 (3*S*,4*S*)-*N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-4-amino-3-hydroxy-5-phenylpentanoate methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-aminohex-4-enoate methyl ester
- 40 *N*-[*N*-(cyclopropylacetyl)-L-alaninyl]-L-phenylglycine *tert*-butyl ester
- N*-*tert*-butyl-*N*'-[*N*-(3,5-Difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-2-(4-phenylphenyl)acetamide
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- N*-[*N*-(3,5-difluorophenylacetyl)-(S)-2-aminobutanoyl]-L-phenylglycine  
*tert*-Butyl Ester
- 5      *N*-[*N*-(3,5-difluorophenylacetyl)-L-valinyl]-L-phenylglycine *tert*-butyl  
ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-methioninyl]-L-phenylglycine methyl  
ester
- 10      *N*-[*N*-(3,5-difluorophenylacetyl)-L-valinyl]-L-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-2-aminobutanoyl]-L-phenylglycine  
methyl ester
- 15      *N*-[*N*-(3,5-difluorophenylacetyl)-L-leucinyl]-L-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-phenylalaninyl]-L-phenylglycine  
methyl ester
- 20      *N*-[*N*-(3,5-difluorophenylacetyl)glycinyl]-L-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-phenylglycinyl]-L-phenylglycine  
methyl ester
- 25      *N*-[*N*-(phenylacetyl)-L-alaninyl]-L-alanine methyl ester
- N*-[*N*-(phenylacetyl)-L-alaninyl]-L-leucine methyl ester
- N*-[*N*-(phenylacetyl)-L-alaninyl]-L-isoleucine methyl ester
- 30      *N*-[*N*-(phenylacetyl)-L-alaninyl]-L-proline methyl ester
- N*-[*N*-(phenylacetyl)-L-alaninyl]-L-phenylalanine methyl ester
- 35      *N*-[*N*-(phenylacetyl)-L-alaninyl]-*N*-(*tert*-butoxycarbonyl)-L-lysine methyl  
ester
- N*-[*N*-(phenylacetyl)-L-alaninyl]-glycine methyl ester
- 40      *N*-[*N*-(phenylacetyl)-L-alaninyl]-L-valine methyl ester
- N*-[*N*-(phenylacetyl)-L-alaninyl]-(S)-2-aminobutanoate methyl ester
- N*-[*N*-(phenylacetyl)-L-alaninyl]-(S)-2-aminopentanoate methyl ester
- 45      *N*-[*N*-(3-nitrophenylacetyl)-L-alaninyl]-L-valine

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- N*-[*N*-(phenylacetyl)-*L*-alaninyl]-*L*-*N*-methylalanine methyl ester
- N*-[*N*-(isovaleryl)-*L*-phenylglycinyl]-*L*-alanine *iso*-butyl ester
- 5      *N*-[*N*-(isovaleryl)-*L*-isoleucinyl]-*L*-alanine *iso*-butyl ester
- N*-Cyclohexyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylglycinamide
- 10      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-4-hydroxyproline ethyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-lysine methyl ester
- 15      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-glutamide
- 1-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]piperidine-2-carboxylate methyl ester
- 20      *N*-[(*S*)-3-hydroxy-6-methylhept-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[(*S*)-2-hydroxy-1-phenyleth-1-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 25      *N*-[*N*-(3,5-difluorophenyl- $\alpha$ -fluoroacetyl)-*L*-alaninyl]-*L*-phenylglycine *tert*-butyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-2-(*S*)-aminocyclohexylacetyl]-*L*-phenylglycine methyl ester
- 30      *N*-[(1*R*,2*S*)-1-hydroxy-1-phenylprop-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 35      *N*-[(1*R*,2*S*)-1-hydroxy-1,2-diphenyleth-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[(1*S*,2*R*)-1-hydroxy-1-phenylprop-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 40      *N*-2-methoxyethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-glycinamide
- 45      *N*-[(*S*)- $\alpha$ -hydroxy- $\alpha$ -phenyl-*iso*-propyl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide

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- N*-[(*S*)-2-hydroxy-1,2-diphenylethyl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 5 *N*-[(*S*)-1-hydroxyhex-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[ $\alpha$ -hydroxy- $\alpha'$ -(4-hydroxyphenyl)-*iso*-propyl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 10 *N*-2-pyridylmethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylalaninamide
- N*-[ $\alpha$ -hydroxy- $\alpha'$ -pyrid-2-yl-*iso*-propyl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 15 *N*-[ $\alpha$ -hydroxy- $\alpha'$ -pyrid-4-yl-*iso*-propyl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[(*S*)-1-hydroxy-4-methylpent-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 20 *N*-[ $\alpha$ -methoxy-prop-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[1-hydroxy-3-methyl-but-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 25 *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-2-amino-2-(6-aminopyrid-2-yl)acetate methyl ester
- N*-[1-hydroxy-prop-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 30 *N*-[(*S*)-2-methoxy-1-phenyleth-1-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[(*S*)-1-methoxy-2-phenyl-prop-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 35 *N*-[(*S*)-1-acetoxylhex-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[(*S*)-1-(*tert*-butylcarbonyloxy)-hex-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 40 *N*-[2-hydroxy-1-(thien-2-yl)ethyl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 45 *N*-[(*S*)-2-hydroxy-2-methyl-1-phenylprop-1-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide

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- N*-[*N*-(3,5-difluorophenylacetyl)-L-(thien-2-yl)glyciny]-L-phenylalanine  
*tert*-butyl ester
- 5      *N*-[*N*-(3,5-difluorophenylacetyl)-L-phenylglyciny]-L-phenylglycinol
- N*-[*N*-(cyclopropaneacetyl)-L-phenylglyciny]-L-phenylglycinol
- N*-[*N*-(cyclopentaneacetyl)-L-phenylglyciny]-L-phenylglycinol
- 10      *N*-[*N*-(3,5-difluorophenylacetyl)-D,L-phenylglyciny]-D,L-phenylglycinamide
- N*-[*N*-(3,5-difluorophenylacetyl)-D,L-valiny]-D,L-phenylglycinamide
- 15      *N*-[*N*-(2-thienylacetyl)-L-alaniny]-L-phenylglycinamide
- N*-[*N*-(*n*-caprotyl)-L-alaniny]-L-phenylglycinamide
- 20      *N*-[*N*-(3,5-difluorophenylacetyl)-L-norleuciny]-L-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-norvaliny]-L-phenylglycine methyl ester
- 25      *N*-[*N*-(3,5-difluorophenylacetyl)-L-*tert*-leuciny]-L-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-isoleuciny]-L-phenylglycine methyl ester
- 30      *N*-[*N*-(3,5-difluorophenylacetyl)-L-cyclohexylalaniny]-L-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-(S)-2-amino-2-(cyclopropyl)acetyl]-L-phenylglycine methyl ester
- 35      *N*-[*N*-(3,5-difluorophenylacetyl)-(S)-2-amino-2-(thien-3-yl)acetyl]-L-phenylglycine methyl ester
- 40      *N*-[*N*-(3,5-difluorophenylacetyl)-(S)-2-amino-2-(thien-2-yl)acetyl]-L-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-(4-fluorophenyl)glyciny]-L-phenylglycine methyl ester
- 45

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- N*-[*N*-(3,5-difluorophenylacetyl)-*D*-(4-fluorophenyl)glyciny]-*L*-phenylglycine methyl ester
- 5 *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-(4-methoxyphenyl)glyciny]-*L*-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-phenylglyciny]-*L*-phenylglycine *tert*-butyl ester
- 10 *N*-[*N*-(cyclopropylacetyl)-*L*-phenylglyciny]-*L*-phenylglycine *tert*-butyl ester
- N*-[*N*-(cyclopentylacetyl)-*L*-phenylglyciny]-*L*-phenylglycine *tert*-butyl ester
- 15 *N*-[*N*-(*tert*-butylacetyl)-*L*-alaniny]-*L*-phenylglycinamide
- N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*L*-(5-bromothien-2-yl)glycinamide
- 20 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*D*-(5-bromothien-2-yl)glycinamide
- N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*L*-(4-bromothien-2-yl)glycinamide
- 25 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*L*-(thien-2-yl)glycinamide
- 30 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*D*-(thien-2-yl)glycinamide
- N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*L*-(thien-3-yl)glycinamide
- 35 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*D*-(thien-2-yl)glycinamide
- N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*D*-phenylglycinamide
- 40 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*L*-phenylglycinamide
- 45 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaniny]-*D,L*-(5-chlorothien-2-yl)glycinamide

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- N*-Cyclohexyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D-4-(phenyl)phenylglycinamide
- 5 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-3-(phenoxy)phenylglycinamide
- 10 *N*-(S)-(-)- $\alpha$ -methylbenzyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- 15 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-(ethyl)phenylglycinamide
- 20 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-2-(benzyl)phenylglycinamide
- 25 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-(cyclohexyl)phenylglycinamide
- 30 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-(4-ethylphenyl)phenylglycinamide
- 35 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-4-(*tert*-butyl)phenylglycinamide
- 40 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-3-(4-chlorophenoxy)phenylglycinamide
- 45 *N*-cyclohexyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-(phenyl)phenylglycinamide
- 40 *N*-[*N*-(3,5-difluorophenyl- $\alpha$ -hydroxyacetyl)-L-alaninyl]-L-phenylglycine *tert*-butyl ester
- 45 *N*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenyl- $\alpha,\alpha$ -difluoroacetyl)-L-alaninyl]-L-phenylglycinamide

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- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*-phenylglycine *tert*-butyl ester
- 5      *N*-[(*S*)-1-oxo-1-phenylprop-2-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-(pyrid-3-yl)glycine *tert*-butyl ester
- 10      [*N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinyl]morpholine
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-(2-methoxy)phenylglycine methyl ester
- 15      *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycine *N-tert*-butoxycarbonyl(hydroxyl amine) ester
- N*-neopentyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinamide
- 20      *N*-tetrahydrofurfuryl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinamide
- N*-methoxy-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinamide
- 25      [*N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinyl]azetidine
- 30      *N-iso*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinamide
- N*-cyclopropanemethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinamide
- 35      *N*-methoxy-*N*-methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinamide
- N*-2-methylprop-2-enyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinamide
- 40      *N*-(pyrid-3-yl)methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D*,*L*-phenylglycinamide
- 45

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- N*-(pyrid-4-yl)methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- 5      *N*-furfuryl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- N*-cyclopentyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- 10      *N*-1-benzylpiperidin-4-yl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- N,N*-dimethyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- 15      *N*-2,2,6,6-tetramethylpiperidin-4-yl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- N*-2-methylcyclohexyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- 20      *N*-4-methylcyclohexyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- N*-1-ethoxycarbonylpiperidin-4-yl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- 25      *N*-methyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- 30      *N-tert*-butoxy-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycine *N-tert*-butyl(hydroxylamine) ester
- 35      *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycine hydrazide
- N*-(1-ethoxyethen-1-yl)-[*N'*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycine hydrazide
- 40      *N*-[*N*-(phenylacetyl)-L-alaninyl]-L-phenylglycine *tert*-butyl ester
- N*-4-(phenyl)butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- 45



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- N*-3-(4-iodophenoxy)propyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- 5 *N*-6-(amino)hexyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycinamide Hydrochloride
- N*-1-(phthalimido)pent-2-yl-*N'*-(3,5-difluorophenylacetyl)-L-alaninamide
- 10 *N*-[*N*-(3,5-difluorophenylacetyl)-L-(3,5-difluorophenyl)glycinyl]-L-(3,5-difluorophenyl)glycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-norleucine
- 15 *N*-[*N*-(cyclopentaneacetyl)-L-alaninyl]-L-phenylglycine *tert*-butyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-fluorophenylglycine *iso*-propyl ester
- 20 *N*-(isopropyl) *N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- N*-[*N*-(cyclopentylacetyl)-L-alaninyl]-L-phenylalanine *tert*-butyl ester
- 25 *N*-[*N*-(cyclopropylacetyl)-L-alaninyl]-L-phenylalanine *tert*-butyl ester
- N*-[*N*-(3,5-Difluorophenylacetyl)-L-alaninyl]-L-phenylglycine *iso*-butyl ester
- 30 *N*-[*N*-(3,5-Difluorophenylacetyl)-L-alaninyl]-D-phenylglycine methyl ester
- N*-[*N*-(3,5-Difluorophenylacetyl)-L-alaninyl]-L-(3- $\alpha$ -phenyl)proline methyl ester
- 35 *N*-[*N*-(3,5-Difluorophenylacetyl)-L-alaninyl]-L-azetidine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-2-amino-3-(5-chlorobenzothiophen-2-yl)acetate methyl ester
- 40 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-3-(thiazol-4-yl)propionate *tert*-butyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide *tert*-butyl ester
- 45 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D-(thien-2-yl)glycinamide

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- N*-[*N*-(3,4-dichlorophenylacetyl)-L-alaninyl]-D-phenylglycinamide
- 5 *N*-[*N*-(3-chlorophenylacetyl)-L-alaninyl]-D-phenylglycinamide
- N*-[*N*-(3-bromophenylacetyl)-L-alaninyl]-D-phenylglycinamide
- N*-[*N*-(3-fluorophenylacetyl)-L-alaninyl]-D-phenylglycinamide
- 10 *N*-[*N*-(4-fluorophenylacetyl)-L-alaninyl]-D-phenylglycinamide
- N*-[*N*-(3-methylphenylacetyl)-L-alaninyl]-D-phenylglycinamide
- 15 *N*-[*N*-(4-methylphenylacetyl)-L-alaninyl]-D-phenylglycinamide
- N*-[*N*-(3-trifluoromethylphenylacetyl)-L-alaninyl]-D-phenylglycinamide
- N*-[*N*-(3-methoxyphenylacetyl)-L-alaninyl]-D-phenylglycinamide
- 20 *N*-[*N*-(2-chlorophenylacetyl)-L-alaninyl]-D-phenylglycinamide
- N*-[*N*-(1-naphthylacetyl)-L-alaninyl]-D-phenylglycinamide
- N*-[*N*-(2-naphthylacetyl)-L-alaninyl]-D-phenylglycinamide
- 25 *N*-[*N*-(phenylacetyl)-L-alaninyl]-D-phenylglycinamide
- N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D-phenylglycine
- 30 *N*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D-phenylglycinamide
- N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-(S)-2-amino-2-(2-furanyl)acetamide
- 35 *N'*-[*N*-(3,5-difluorophenylacetyl)-D-alaninyl]-D-phenylglycinamide
- N'*-[*N*-(3,4-difluorophenylacetyl)-D-alaninyl]-D-phenylglycinamide
- 40 *N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylalanin-N-methylsulfonamide
- N''*-methyl-*N''*-phenyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-glycinamide
- 45 *N''*-methyl-*N''*-phenyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-alaninamide

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- N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-methioninyl]-*L*-phenylglycinamide
- 5 *N''*-methyl-*N''*-benzyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-glycinamide
- N''*-4-fluorobenzyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylglycinamide
- 10 *N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-(4-fluoro)phenylglycine neopentyl ester
- N*-[*N*-(2,3,4,5,6-pentafluorophenylacetyl)-*L*-alaninyl]-*L*-(pyrid-3-yl)glycine methyl ester
- 15 *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-(pyrid-3-yl)glycine *tert*-butyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-(*O*-benzyl)serinyl]-*L*-phenylglycine methyl ester
- 20 *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-(*O*-benzyl)threoninyl]-*L*-phenylglycine methyl ester
- N*-[*N*-(3,5-difluorophenylacetyl)-*L*-threoninyl]-*L*-phenylglycine methyl ester
- 25 *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-serinyl]-*L*-phenylglycine methyl ester
- N''*-4-methylphenyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylglycinamide
- 30 *N''*-tetrahydrofurfuryl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylglycinamide
- N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-4-fluorophenylglycinamide
- 35 *N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-methionyl]-*L*-phenylglycinamide
- 40 *N*-[*N*-(3,5-difluorophenylacetyl)-2-aminobutanoyl]-*L*-phenylglycinamide
- N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-phenylglycinyl]-*L*-phenylglycinamide
- 45 *N*-[*N*-(3,5-difluorophenylacetyl)-*L*-valinyl]-*L*-phenylglycinamide

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- N*-[(*R*)- $\alpha$ -methylbenzyl]-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- 5      *N*-[1-phenyl-2-oxo-3-methylbutan-1-yl]-*N'*-(3,5-difluorophenylacetyl)-L-alaninamide
- 10      *N*-[1-phenyl-2-oxo-propan-1-yl]-*N'*-(3,5-difluorophenylacetyl)-L-alaninamide
- 15      *N*-[1-phenyl-2-oxo-2-phenyl-ethan-1-yl]-*N'*-(3,5-difluorophenyl-acetyl)-L-alaninamide
- 20      *N*-[1-phenyl-2-oxo-4-methylpentan-1-yl]-*N'*-(3,5-difluorophenyl-acetyl)-L-alaninamide
- 25      *N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L- $\alpha$ -hydroxyphenylalanine methyl ester
- 30      *N''*-[4-((2-hydroxy-4-azido)-phenyl)-NHC(O)-)butyl] *N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-phenylglycinamide
- 35      *N*-[(*S*)-1-phenyl-2-oxo-2-phenyl-ethan-1-yl]-*N'*-(3,5-difluorophenyl-acetyl)-L-alaninamide
- 40      *N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-fluorophenylglycine *tert*-butyl ester
- 45      *N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-phenylphenylglycine *tert*-butyl ester
- [*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-(2,3-benzo[b]proline) methyl ester
- N''*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-L-4-*n*-butylphenylglycinamide
- N''*-*tert*-butyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-4-(phenylacetenyl)phenylglycinamide
- N'*-[*N*-(3,5-difluorophenylacetyl)-L-alaninyl]-D,L-phenylglycynthioamide

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- N*-[1,3-diphenyl-2-oxo-propan-1-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 5 *N*-[1-phenyl-2-oxo-2-cyclopentylethan-1-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N*-[1-phenyl-2-oxo-hexan-1-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 10 *N*-[1-phenyl-2-oxo-3-methylpentan-1-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- N''*-*n*-hexyl-6-biotinamidyl-*N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D,L*-phenylglycinthioamide
- 15 *N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-methioninyl]-*L*-methionine
- N'*-[*N*-(2-*tert*-BOC-amino)propionyl]-*L*-alaninyl]-*L*-phenylglycine methyl ester
- 20 *N''*-*tert*-butyl *N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-2-fluorophenylglycinamide
- N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-alaninyl]-*D,L*-2-phenylglycine methyl ester
- 25 *N*-[(*S*)-1-phenyl-2-oxo-3-phenylpropan-1-yl]-*N'*-(3,5-difluorophenylacetyl)-*L*-alaninamide
- 30 *N'*-[*N*-(3,5-difluorophenylacetyl)-*D,L*-thien-3-ylglycinyl]-*D,L*-2-phenylglycine
- N'*-[*N*-(3,5-difluorophenylacetyl)-*D,L*-thien-3-ylglycinyl]-*D,L*-2-phenylglycine *tert*-butyl ester
- 35 *N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-thien-3-ylglycinyl]-*L*-2-phenylglycine
- N'*-[*N*-(3,5-difluorophenylacetyl)-*L*-thien-3-ylglycinyl]-*L*-2-phenylglycine *tert*-butyl ester
- 40 *N*-[2-hydroxy-1-(*S*)phenyleth-1-yl]-*N'*-[(3,5-difluorophenylacetyl)-*L*-phenylglycinyl]-*L*-alaninamide
- N*-[2-hydroxyeth-1-yl]-*N'*-[(3,5-difluorophenylacetyl)-*L*-alaninyl]-*L*-phenylglycinamide
- 45

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*N'*-[*N*-(3,5-difluorophenyl-2-oxo-acetyl)-L-alaninyl]-L-2-phenylglycine  
*tert*-butyl ester

[*N*-(2,5-dichlorophenoxyacetyl)-L-alaninyl]-L-phenylglycine methyl ester

[*N*-(3,5-difluorophenoxyacetyl)-L-alaninyl]-L-phenylglycine methyl ester

[*N*-(3,4-dichlorothiophenoxyacetyl)-L-alaninyl]-L-phenylglycine methyl  
ester

[*N*-(3-aminopropionyl)-L-alaninyl]-L-phenylglycine *tert*-butyl ester

[*N*-(3-*tert*-butoxycarbonylamino)propionyl)-L-alaninyl]-L-phenylglycine  
*tert*-butyl ester

The pharmaceutical compositions described above comprise a  
pharmaceutically inert carrier and a compound of the formula I above.

In formula I above, X'' is preferably hydrogen and X' is preferably  
hydrogen or fluoro.

In formula I above, Z is preferably a covalent bond linking R<sup>1</sup> to  
-CX'X''-.

In formula I above, preferred R<sup>1</sup> unsubstituted aryl groups include, for  
example, phenyl, 1-naphthyl, 2-naphthyl, and the like.

Preferred R<sup>1</sup> substituted aryl groups include, for example, monosubsti-  
tuted phenyls (preferably 3 or 5 substituents); disubstituted phenyls (preferably  
3,5 substituents); and trisubstituted phenyls (preferably 3,4,5 substituents).  
Preferably, the substituted phenyl groups do not include more than 3  
substituents.

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Examples of substituted phenyls include, for instance, 4-fluorophenyl, 4-chlorophenyl, 4-bromophenyl, 4-nitrophenyl, 4-methylphenyl, 3-methoxyphenyl, 3-nitrophenyl, 3-fluorophenyl, 3-chlorophenyl, 3-bromophenyl, 3-thiomethoxyphenyl, 3-methylphenyl, 3-trifluoromethylphenyl, 2-hydroxyphenyl, 2-methylphenyl, 2-fluorophenyl, 2-chlorophenyl, 3,4-difluorophenyl, 2,3,4,5,6-pentafluorophenyl, 3,4-dibromophenyl, 3,4-dichlorophenyl, 3,4-methylene-dioxyphenyl, 3,5-difluorophenyl, 3,5-dichlorophenyl, 2,4-dichlorophenyl, and 2,5-difluorophenyl.

10 Preferred R<sup>1</sup> alkaryl groups include, by way of example, benzyl, 2-phenylethyl, 3-phenyl-*n*-propyl, and the like.

Preferred R<sup>1</sup> alkyl, substituted alkyl, alkenyl, cycloalkyl and cycloalkenyl groups include, by way of example, *iso*-propyl, *n*-propyl, *n*-butyl, *iso*-butyl, *sec*-butyl, *tert*-butyl, -CH<sub>2</sub>CH=CH<sub>2</sub>, -CH<sub>2</sub>CH=CH(CH<sub>2</sub>)<sub>4</sub>CH<sub>3</sub>, cyclopropyl, cyclobutyl, cyclohexyl, cyclopentyl, cyclohex-1-enyl, -CH<sub>2</sub>-cyclopropyl, -CH<sub>2</sub>-cyclobutyl, -CH<sub>2</sub>-cyclohexyl, -CH<sub>2</sub>-cyclopentyl, -CH<sub>2</sub>CH<sub>2</sub>-cyclopropyl, -CH<sub>2</sub>CH<sub>2</sub>-cyclobutyl, -CH<sub>2</sub>CH<sub>2</sub>-cyclohexyl, -CH<sub>2</sub>CH<sub>2</sub>-cyclopentyl, aminomethyl, *N-tert*-butoxycarbonylaminomethyl, and the like.

20 Preferred R<sup>1</sup> heteroaryls and substituted heteroaryls include, by way of example, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, fluoropyridyls (including 5-fluoropyrid-3-yl), chloropyridyls (including 5-chloropyrid-3-yl), thien-2-yl, thien-3-yl, benzothiazol-4-yl, 2-phenylbenzoxazol-5-yl, furan-2-yl, benzofuran-2-yl, thionaphthen-2-yl, 2-chlorothiophen-5-yl, 3-methylisoxazol-5-yl, 2-(thiophenyl)thiophen-5-yl, 6-methoxythionaphthen-2-yl, 3-phenyl-1,2,4-thioxadiazol-5-yl, 2-phenyloxazol-4-yl, and the like.

30 Preferably R<sup>2</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl and heterocyclic. Particularly preferred R<sup>2</sup> substituents include, by way of example, methyl, ethyl, *n*-propyl,

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*iso*-propyl, *n*-butyl, *iso*-butyl, *sec*-butyl, phenyl, 4-fluorophenyl, 3,5-difluorophenyl, 4-methoxyphenyl, benzyl, cyclopropyl, cyclohexyl, cyclopentyl, cycloheptyl, thien-2-yl, thien-3-yl, -CH<sub>2</sub>CH<sub>2</sub>SCH<sub>3</sub>, -CH<sub>2</sub>OCH<sub>2</sub>φ, -CH(CH<sub>3</sub>)OCH<sub>2</sub>φ, -CH(OH)CH<sub>3</sub>, -CH<sub>2</sub>OH and the like. As noted below, R<sup>2</sup> (as well as R<sup>4</sup>) is preferably the side chain of an L-amino acid.

Preferably, R<sup>3</sup> is hydrogen, methyl or together with R<sup>4</sup> and the nitrogen to which R<sup>3</sup> is attached forms pyrrolidin-2-yl, 2,3-dihydroindol-2-yl, piperidin-2-yl, 4-hydroxy-pyrrolidin-2-yl, 1,2,3,4-tetrahydroisoquinolin-3-yl, and the like.

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Preferred R<sup>4</sup> substituents include, for example, hydrogen, methyl, ethyl, *iso*-propyl, *n*-propyl, *n*-butyl, *sec*-butyl, *iso*-butyl, cyclopentyl, cyclohexyl, allyl, *iso*-but-2-enyl, 3-methylpentyl, -CH<sub>2</sub>-cyclopropyl, -CH<sub>2</sub>-cyclohexyl, -CH<sub>2</sub>-indol-3-yl, phenyl, *p*-(phenyl)phenyl, *m*-(phenyl)phenyl *o*-fluorophenyl, *m*-fluorophenyl, *p*-fluorophenyl, *p*-bromophenyl, *m*-methoxyphenyl, *p*-methoxyphenyl, phenethyl, benzyl, *m*-hydroxybenzyl, *p*-hydroxybenzyl, *p*-nitrobenzyl, *m*-trifluoromethylphenyl, *p*-(CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O-benzyl, *p*-(CH<sub>3</sub>)<sub>3</sub>COC(O)CH<sub>2</sub>O-benzyl, *p*-phenylphenyl, 3,5-difluorophenyl, *p*-(HOOCCH<sub>2</sub>O)-benzyl, 2-aminopyrid-6-yl, 4-(N-morpholino-CH<sub>2</sub>CH<sub>2</sub>O)-benzyl, -CH<sub>2</sub>CH<sub>2</sub>C(O)NH<sub>2</sub>, -CH<sub>2</sub>-imidazol-4-yl, -CH<sub>2</sub>-(3-tetrahydrofuran-2-yl), -CH<sub>2</sub>-thien-2-yl, -CH<sub>2</sub>-thiazol-4-yl, -CH<sub>2</sub>-(1-methyl)cyclopropyl, -CH<sub>2</sub>-thien-3-yl, thien-3-yl, thien-2-yl, -CH<sub>2</sub>-C(O)O-*t*-butyl, -CH<sub>2</sub>-C(CH<sub>3</sub>)<sub>3</sub>, -CH<sub>2</sub>CH(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>, 2-methylcyclopentyl, -cyclohex-2-enyl, -CH[CH(CH<sub>3</sub>)<sub>2</sub>]COOCH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub>SCH<sub>3</sub>, -CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>C(CH<sub>3</sub>)=CH<sub>2</sub>, -CH<sub>2</sub>CH=CHCH<sub>3</sub> (*cis* and *trans*), -CH<sub>2</sub>OH, -CH(OH)CH<sub>3</sub>, -CH(O-*t*-butyl)CH<sub>3</sub>, -CH<sub>2</sub>OCH<sub>3</sub>, -(CH<sub>2</sub>)<sub>4</sub>NH-Boc, -(CH<sub>2</sub>)<sub>4</sub>NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>4</sub>N(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>-pyridyl (e.g., 2-pyridyl, 3-pyridyl and 4-pyridyl), pyridyl (2-pyridyl, 3-pyridyl and 4-pyridyl), -CH<sub>2</sub>-naphthyl (e.g., 1-naphthyl and 2-naphthyl), -CH<sub>2</sub>-(N-morpholino), *p*-(N-morpholino-CH<sub>2</sub>CH<sub>2</sub>O)-benzyl, benzo[b]thiophen-2-yl, benzo[b]thiophen-3-yl, 5-chlorobenzo[b]thiophen-2-yl, 4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl,

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benzo[b]thiophen-3-yl, tetrazol-5-yl, 5-chlorobenzo[b]thiophen-3-yl, benzo[b]thiophen-5-yl, 6-methoxynaphth-2-yl, -CH<sub>2</sub>-N-phthalimidyl, 2-methylthiazol-4-yl, and thieno[2,3-*b*]thiophen-2-yl, 5-bromothien-2-yl, 4-bromothien-2-yl, 5-chlorothien-2-yl, 3-phenoxyphenyl, 2-phenoxyphenyl, 4-ethylphenyl, 2-benzylphenyl, (4-ethylphenyl)phenyl, 4-*tert*-butylphenyl, 4-*n*-butylphenyl, *o*-(4-chlorophenoxy)phenyl, furan-2-yl, 4-phenylacetylenylphenyl and the like.

Preferably, R<sup>5</sup> is hydrogen. However, in another embodiment, R<sup>4</sup> and R<sup>5</sup> are fused to form a cycloalkyl group including, for example, cyclopropyl, cyclobutyl, and the like.

One preferred X substituent is -C(O)Y. Preferably Y is hydroxy, alkoxy or substituted alkoxy such as methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *iso*-butoxy, *tert*-butoxy, *neo*-pentoxy, benzyloxy, 2-phenylethoxy, 3-phenyl-*n*-propoxy, 3-iodo-*n*-propoxy, 4-bromo-*n*-butoxy, -ONHC(O)OC(CH<sub>3</sub>)<sub>3</sub>, -ONHC(CH<sub>3</sub>)<sub>3</sub> and the like. Another preferred Y group is -NR'R'' where R' and R'' are as defined above. Such preferred Y groups include, by way of example, amino (-NH<sub>2</sub>), -NH(*iso*-butyl), -NH(*sec*-butyl), N-methylamino, N,N-dimethylamino, N-benzylamino, N-morpholino, azetidino, N-thiomorpholino, N-piperidinyl, N-hexamethyleneimino, N-heptamethylene-imino, N-pyrrolidinyl, -NH-methallyl, -NHCH<sub>2</sub>-(furan-2-yl), -NHCH<sub>2</sub>-cyclopropyl, -NH(*tert*-butyl), -NH(*p*-methylphenyl), -NHOCCH<sub>3</sub>, -NHCH<sub>2</sub>(*p*-fluorophenyl), -NHCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, -NH-cyclopentyl, -NH-cyclohexyl, -NHCH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -NHCH<sub>2</sub>C(CH<sub>3</sub>)<sub>3</sub>, -NHCH<sub>2</sub>-(pyrid-2-yl), -NHCH<sub>2</sub>-(pyrid-3-yl), -NHCH<sub>2</sub>-(pyrid-4-yl), N-thiazolindinyl, -N(CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>, -N[CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>]<sub>2</sub>, -NHOH, -NH(*p*-NO<sub>2</sub>-φ), -NHCH<sub>2</sub>(*p*-NO<sub>2</sub>-φ), -NHCH<sub>2</sub>(*m*-NO<sub>2</sub>-φ), -N(CH<sub>3</sub>)OCH<sub>3</sub>, -N(CH<sub>3</sub>)CH<sub>2</sub>-φ, -NHCH<sub>2</sub>-(3,5-di-fluorophenyl), -NHCH<sub>2</sub>CH<sub>2</sub>F, -NHCH<sub>2</sub>(*p*-CH<sub>3</sub>O-φ), -NHCH<sub>2</sub>(*m*-CH<sub>3</sub>O-φ), -NHCH<sub>2</sub>(*p*-CF<sub>3</sub>-φ), -N(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, -NHCH<sub>2</sub>CH<sub>2</sub>φ, -NHCH(CH<sub>3</sub>)φ, -NHCH<sub>2</sub>-(*p*-F-φ), -N(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -NHCH<sub>2</sub>-(tetrahydrofuran-2-yl), -NHCH<sub>2</sub>(*p*-trifluoromethylphenyl),

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-NHCH<sub>2</sub>C(CH<sub>3</sub>)=CH<sub>2</sub>, -NH-[(*p*-benzyl)pyrid-4-yl], -NH-[(2,6-dimethyl)pyrid-4-yl], -NH-(2-methylcyclohexyl), -NH-(4-methylcyclohexyl),  
 -NH-[N-ethoxycarbonyl]-piperidin-4-yl, -NHOC(CH<sub>3</sub>)<sub>3</sub>, -NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>- $\phi$ ,  
 -C(O)NH(CH<sub>2</sub>)<sub>3</sub>O-(*p*-CH<sub>3</sub>) $\phi$ , -C(O)NH(CH<sub>2</sub>)<sub>6</sub>NH<sub>2</sub>, -NH-(tetrahydrofuran-2-yl),  
 5 -N(CH<sub>3</sub>) $\phi$ , -NH(CH<sub>2</sub>)<sub>4</sub>NHC(O)-(2-hydroxy-4-azido)-phenyl, -NH(CH<sub>2</sub>)<sub>6</sub>-  
 (biotinamidyl), and the like.

Another preferred Y group is an alkyl group such as methyl, ethyl,  
*iso*-propyl, *n*-propyl, *iso*-butyl, *n*-butyl, *sec*-butyl, *tert*-butyl,  
 10 -CH<sub>2</sub>CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>-pyridyl-2-yl, -CH<sub>2</sub>-pyridyl-3-yl, -CH<sub>2</sub>-pyridyl-4-yl,  
 -CH<sub>2</sub>-fur-2-yl, and the like; a substituted alkyl group such as benzyl; a  
 cycloalkyl group such as cyclopentyl; and an aryl group such as phenyl.

Still another preferred Y group is -NHSO<sub>2</sub>-R where R is selected from  
 15 alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, aryl, heteroaryl  
 and heterocyclic. Such groups are exemplified by NH-SO<sub>2</sub>-CH<sub>3</sub>.

Preferred Y' groups include a substituted alkyl group such as  
 -CH<sub>2</sub>OH, -CH(OH)CH<sub>2</sub>CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, -CH(OH) $\phi$ , -CH(OH)CH<sub>2</sub>C(O)OCH<sub>3</sub>,  
 20 -C(OH)(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>OCH<sub>3</sub>, -CH<sub>2</sub>OC(O)OCH<sub>3</sub>, -CH<sub>2</sub>OC(O)C(CH<sub>3</sub>)<sub>3</sub>, and the  
 like.

Preferred compounds for use in the methods of this invention include  
 those set forth in the tables below: